FILE 'HOME' ENTERED AT 18:04:40 ON 19 MAR 2003

=> file medline caplus cancerlit embase biosis
COST IN U.S. DOLLARS
SINCE FILE TOTAL
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SESSION
FULL ESTIMATED COST
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FILE 'MEDLINE' ENTERED AT 18:05:05 ON 19 MAR 2003

FILE 'CAPLUS' ENTERED AT 18:05:05 ON 19 MAR 2003
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FILE 'BIOSIS' ENTERED AT 18:05:05 ON 19 MAR 2003
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=> s sepsis or septicemia or septic (W) disorder
L1 154301 SEPSIS OR SEPTICEMIA OR SEPTIC (W) DISORDER

=> s interleukin-6 or 1l-6
L2 119260 INTERLEUKIN-6 OR 1L-6

=> s l1 (s) l2
L3 1955 L1 (S) L2

=> s serum (w) levels
L4 122388 SERUM (W) LEVELS

=> s l3 (s) l4
L5 137 L3 (S) L4

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, CANCERLIT, EMBASE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L5
L6 43 DUPLICATE REMOVE L5 (94 DUPLICATES REMOVED)

=> d l6 1- ibib,abs
YOU HAVE REQUESTED DATA FROM 43 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 43 MEDLINE
DUPLICATE 1
ACCESSION NUMBER: 2003003128 MEDLINE
DOCUMENT NUMBER: 22386813
PubMed ID: 12500222
TITLE: Elevated serum levels of the type I and type II receptors
for tumor necrosis factor-alpha as predictive factors for
ARF in patients with septic shock.
AUTHOR: Iglesias Jose; Marik Paul E; Levine Jerrold S
CORPORATE SOURCE: Department of Internal Medicine, Robert Wood Johnson School
of Medicine, Neptune, NJ, USA. (Norasept II Study
Investigators).
miglesias@erols.com
CONTRACT NUMBER: DK59793 (NIDDK)
HL69722 (NHLBI)
SOURCE: AMERICAN JOURNAL OF KIDNEY DISEASES, (2003 Jan) 41 (1)
62-75.
Journal code: 8110075. ISSN: 1523-6838.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20030103
Last Updated on STN: 20030118
Entered Medline: 20030117
AB BACKGROUND: Acute renal failure (ARF), a common and serious complication
in patients with septic shock, has high mortality. Recent data suggest

that proinflammatory cytokines may contribute to sepsis -associated ARF. METHODS: To examine the role of proinflammatory cytokines, we evaluated 537 patients enrolled in the placebo arm of the Norasept II study, of whom 112 patients (20%) developed ARF. RESULTS: By univariate analysis, the following factors were significantly associated with the development of ARF: male sex, younger age, increased heart rate, higher Acute Physiology and Chronic Health Evaluation II score, oliguria, increased blood urea nitrogen level, increased serum creatinine (Scr) level, decreased arterial pH, and increased serum potassium level. Although there were no statistically significant differences in serum levels of tumor necrosis factor-alpha (TNF-alpha) or interleukin-6 between patients with and without ARF, elevated serum levels of the two soluble TNF-alpha receptors (S-TNF-RI and S-TNF-RII) were strongly associated with the development of ARF (S-TNF-RI, 25 +/- 16 versus 18 +/- 13 ng/mL; P = 0.00006; S-TNF-RII, 25 +/- 21 versus 18 +/- 17 ng/mL; P = 0.0007). Using forward stepwise regression analysis, elevated S-TNF-R level remained an independent predictor for ARF, even when we limited our analysis to patients with Scr levels of 1.4 mg/dL or less (< or =124 micromol/L) at study entry, suggesting that decreased renal clearance of S-TNF-R alone cannot account for this association. Elevated S-TNF-R level also was an independent predictor of mortality among patients developing ARF. CONCLUSION: S-TNF-R level is an independent predictor for the development of ARF and mortality. We speculate that elevated S-TNF-R levels may reflect a more intense inflammatory response.

L6 ANSWER 2 OF 43 BIOSIS

ACCESSION NUMBER: 2002:387188 BIOSIS
DOCUMENT NUMBER: PREV200200387188
TITLE: Protective effects of anti-IL-6 antibody treatment in sepsis.
AUTHOR(S): Neff, Thomas A. (1); Riedemann, N. C. (1); Guo, R. F. (1); Laudes, I. (1); Sarma, V. (1); Ward, P. A. (1)
CORPORATE SOURCE: (1) Pathology, University of Michigan, 1301 Catherine St., Ann Arbor, MI, 48109-0602 USA
SOURCE: FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A592. http://www.fasebj.org/. print. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The glycoprotein interleukin-6 plays a key role in the regulation of cell growth and inflammation and in the acute phase reaction during the inflammatory process. It has been demonstrated that IL-6 serum levels are strongly increased during sepsis when compared to healthy individuals. In this study we investigated the effects of anti-IL-6 antibody treatment in cecal ligation and puncture (CLP)-induced sepsis in mice. Animals treated with a monoclonal anti mouse IL-6 antibody administered intravenously directly after CLP showed a dose dependent improved survival, seven days after induction of sepsis when compared to IgG control injected animals. 6 hours after CLP serum levels of IL-6 were significantly decreased in anti-IL-6 treated animals (40 ug/animal) when compared to animals treated with the IgG control. In addition we found evidence that anti-IL-6 treated animals showed low serum

levels of TNFa, 6 hours after CLP, while IgG injected control animals showed no detectible TNFa levels in the serum. The suppression of bioactive IL-6 serum levels in the onset of sepsis may therefore alter the acute inflammatory response with resulting beneficial effects on survival.

L6 ANSWER 3 OF 43 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 2002003486 MEDLINE
DOCUMENT NUMBER: 21623714
PubMed ID: 11750194
TITLE: Early diagnostic markers for neonatal sepsis: comparing C-reactive protein, interleukin-6, soluble tumour necrosis factor receptors and soluble adhesion molecules.
AUTHOR: Dollner H; Vatten L; Austgulen R
CORPORATE SOURCE: Department of Paediatrics, University Hospital of Trondheim, N-7006 Trondheim, Norway..
henrik.dollner@medisin.ntnu.no
SOURCE: JOURNAL OF CLINICAL EPIDEMIOLOGY, (2001 Dec) 54 (12) 1251-7.
Journal code: 8801383. ISSN: 0895-4356.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020102
Last Updated on STN: 20020131
Entered Medline: 20020130
AB We compared six inflammatory mediators (C-reactive protein (CRP), interleukin-6 (IL-6), soluble tumour necrosis factor receptors (p55 and p75) and soluble adhesion molecules (ICAM-1, E-selectin)) as early diagnostic tests for neonatal sepsis, and studied the possible benefit of combining parameters. Blood samples were obtained from 166 consecutively admitted neonates, who were suspected to suffer from infection within the first week of life. Neonates were retrospectively classified as infected (sepsis, clinical sepsis or pneumonia), possibly infected, or non-infected. Twenty-four infected neonates had higher serum levels of all six mediators (all $P < 0.05$), and 18 possibly infected neonates had higher levels of CRP, IL-6, ICAM-1 and E-selectin (all $P < 0.05$), than neonates without infection ($n = 124$). Receiver operator characteristic plots showed that CRP was the single best diagnostic test. Multiple logistic regression modelling, including various combinations of two to six mediators, consistently showed that IL-6, in addition to CRP, predicted sepsis. With infected and possibly infected neonates as the reference standard, a combined test of CRP > or = 10 mg/l and/or IL-6 > or = 20 pg/ml had a sensitivity of 85%, specificity of 62%, and negative likelihood ratio of 0.24. Using infected neonates as reference standard alone, and including possibly infected as controls, sensitivity increased to 96%, whereas specificity decreased to 58%; a negative test result (CRP < 10 mg/l and IL-6 < 20 pg/ml) ruled out sepsis with high certainty (likelihood ratio = 0.07). CRP performed best as a diagnostic test for neonatal sepsis. Diagnostic accuracy was further improved by combining CRP and IL-6, whereas the other parameters (p55, p75, ICAM-1 and E-selectin) added no further diagnostic information.

L6 ANSWER 4 OF 43 MEDLINE
DUPLICATE 3
ACCESSION NUMBER: 2002349110 MEDLINE
DOCUMENT NUMBER: 22087500
PubMed ID: 12092128
TITLE: [Chorioamnionitis and early-onset neonatal sepsis do not significantly affect levels of interleukin-6 in very low birth weight neonates].

Chorioamniitis a casna novorozenecka sepse neovlivnuji vyznamne hladinu interleukinu-6 u novorozencu velmi nizke porodni hmotnosti.
AUTHOR: Janota J; Stranak Z; Belohlavkova S; Jirasek J E
CORPORATE SOURCE: Ustav pro peci o matku a dite, Podolske nabrezi 157, 147 10 Praha 4-Podoli, Czech Republic.
SOURCE: SBORNIK LEKARSKY, (2001) 102 (3) 411-8.
Journal code: 0025770. ISSN: 0036-5327.
PUB. COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Czech
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020703
Last Updated on STN: 20020809
Entered Medline: 20020808
AB OBJECTIVE: To determine the influence of maternal chorioamnionitis and neonatal sepsis on interleukin-6 (IL-6) levels in cord blood and in blood obtained from very low birth weight (VLBW) infants within the first two hours of life. DESIGN: Prospective clinical study. SETTING: Institute for the Care of Mother and Child, Prague. METHODS: We measured the serum levels of IL-6 in 30 consecutive VLBW infants born in our institute. IL-6 levels were evaluated in cord blood and in neonatal blood within 2 hours after delivery. Maternal chorioamnionitis and neonatal sepsis within the first 72 hours of life were monitored. RESULTS: Maternal chorioamnionitis was detected in 7 of 30 patients (23.3%). There was no significant increase in IL-6 level in cord blood of newborns with maternal chorioamnionitis ($p = 0.42$). Serum level of IL-6 in this group did not differ from the level in newborns of mothers without signs of intraamniotic infection ($p = 0.39$). Neonatal early-onset sepsis was diagnosed in 7 of 30 patients (23.3%). There was no influence of neonatal sepsis on IL-6 level in cord blood ($p = 0.98$) and IL-6 level in neonatal blood ($p = 0.19$). We did not find any correlation between the group "chorioamnionitis positive" and "sepsis positive" ($p = 0.31$). CONCLUSION: IL-6 in cord blood or in neonatal blood within 2 hours of life was not enough sensitive and specific marker of maternal chorioamnionitis as well as for early-onset neonatal sepsis in the group of very low birth weight infants.

L6 ANSWER 5 OF 43 CAPLUS
COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 2001:443273 CAPLUS
DOCUMENT NUMBER: 136:181587
TITLE: Detection of cytokine level in cord blood for early diagnosis of neonatal sepsis
AUTHOR(S): Jin, Yalei; Wang, Xueqin; Yu, Liping; Zhang, Yuhou
CORPORATE SOURCE: Department of Pediatrics, Zhongnan Hospital, Wuhan University, Wuhan, 430071, Peop. Rep. China
SOURCE: Wuhan Daxue Xuebao, Yixueban (2001), 22(1), 87-88
CODEN: WDXYAA
PUBLISHER: Wuhan Daxue Jikanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The serum levels of interleukin-6 (IL-6) and tumor necrosis factor-.alpha. (TNF.alpha.) in neonatal sepsis as biomarker for early diagnosis of neonatal sepsis were studied. Serum levels of IL-6 and TNF.alpha. in cord blood of 20 cases with sepsis and 52 healthy controls were detd. by ELISA. The serum level of IL-6 was significantly higher in neonatal sepsis group (0.026 6-1.258 9 ng mL-1) than in control (0.021 1-0.053 1 ng mL-1). The serum level of TNF.alpha. was also significantly higher in neonatal sepsis group (0.65-12.60 ng mL-1) than in control. The results showed that the serum

levels of IL-6 and TNF.alpha. in cord blood can be used as a biomarker of neonatal sepsis, and IL-6 had higher sensitivity and specificity than TNF.alpha..

L6 ANSWER 6 OF 43 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001534619 MEDLINE
DOCUMENT NUMBER: 21465323
PubMed ID: 11581469
TITLE: Reactive hyperemia and interleukin 6, interleukin 8, and tumor necrosis factor-alpha in the diagnosis of early-onset neonatal sepsis.
AUTHOR: Martin H; Olander B; Norman M
CORPORATE SOURCE: Department of Women and Child Health, Division of Neonatology, Karolinska Hospital, Sweden.. helena.martin@kbh.ki.se
SOURCE: PEDIATRICS, (2001 Oct) 108 (4) E61.
Journal code: 0376422. ISSN: 1098-4275.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011003
Last Updated on STN: 20020125
Entered Medline: 20020103
AB OBJECTIVE: To evaluate the diagnostic value of peripheral circulatory reactive hyperemia and serum levels of interleukin-6 (IL-6), IL-8, and tumor necrosis factor-alpha (TNF-alpha) in early-onset neonatal sepsis. METHODS: Reactive hyperemia in the dorsal hand and serum levels of IL-6, IL-8, and TNF-alpha were studied in newborn infants (n = 32; gestational age 39 +/- 3 weeks) who had been admitted to the neonatal unit because of suspected sepsis <48 hours after birth. On admission, reactive hyperemia after a standardized arterial occlusion was measured with laser Doppler technique, and blood samples were taken for cytokine analyses. On the basis of predetermined criteria, the infants subsequently were classified as septic (n = 12) or not (n = 20). RESULTS: The degree of reactive hyperemia was higher in the group with sepsis (median + 170% perfusion increase) than in that without (+37%). On admission, serum levels of IL-6, IL-8, and TNF-alpha all were higher in septic (median values: 1620, 331, and 22 pg/mL, respectively) than in nonseptic neonates (median values: 42, 63, and 13 pg/mL, respectively). In the group with sepsis, the degree of reactive hyperemia correlated to log IL-6 (r = 0.80) and log IL-8 values (r = 0.71). CONCLUSION: Newborn infants with septicemia have increased reactive hyperemia and elevated cytokine levels very early in their disease. Reactive hyperemia in skin can be analyzed at the bedside and noninvasively and therefore may serve as an additional diagnostic tool in neonatal sepsis.

L6 ANSWER 7 OF 43 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001383763 MEDLINE
DOCUMENT NUMBER: 21246625
PubMed ID: 11348793
TITLE: Interleukin-6 and C-reactive protein serum levels in sepsis-related fatalities during the early postmortem period.
AUTHOR: Tsokos M; Reichelt U; Jung R; Nierhaus A; Puschel K
CORPORATE SOURCE: Institute of Legal Medicine, University of Hamburg, Butenfeld 34, D-22529, Hamburg, Germany.. mtsokos@ngi.de
SOURCE: FORENSIC SCIENCE INTERNATIONAL, (2001 Jun 1) 119 (1) 47-56.
Journal code: 7902034. ISSN: 0379-0738.

PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(VALIDATION STUDIES)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

AB Postmortem interleukin-6 (IL-6) and C-reactive protein (CRP) serum levels were investigated prospectively in sepsis-related fatalities and non-septic fatalities by using a linear regression model. At least three blood samples were collected between 0.3 and 139 h postmortem from sepsis-related fatalities (n=8) and non-septic fatalities (n=16). In addition, one antemortem blood sample was collected shortly before death from the septic patients. Antemortem and postmortem IL-6 and CRP levels were highly elevated in all individuals included in the sepsis group. An excessive postmortem increase of IL-6 serum levels associated with progressive time after death was observed in five out of the eight septic patients. Both, IL-6 and CRP serum concentrations seem to be suitable biochemical postmortem markers of sepsis. The determination of IL-6 serum levels above 1500 pg/ml in peripheral venous blood obtained in the early postmortem interval can be considered as a diagnostic hint towards an underlying septic condition. A more precise postmortem discrimination between sepsis and non-septic underlying causes of death is provided by the postmortem measurement of serum CRP in peripheral venous blood: on condition that at least two postmortem CRP values have been determined at different time points postmortem, the CRP level of a deceased at the time of death can be calculated by using linear regression analysis. When assessing postmortem IL-6 and CRP concentrations as biochemical postmortem markers of sepsis, various clinical conditions, such as a preceding trauma or burn injury going along with elevated IL-6 and/or CRP levels prior to death as a result of the systemic inflammatory response syndrome (SIRS) should be taken into consideration, thus adding relevant information for the practical interpretation of the results.

L6 ANSWER 8 OF 43 MEDLINE
DUPLICATE 7
ACCESSION NUMBER: 2001276023 MEDLINE
DOCUMENT NUMBER: 21259571
PubMed ID: 11359438
TITLE: Suppression of the clinical and cytokine response to endotoxin by RWJ-67657, a p38 mitogen-activated protein-kinase inhibitor, in healthy human volunteers.
AUTHOR: Fijen J W; Zijlstra J G; De Boer P; Spanjersberg R; Cohen Tervaert J W; Van Der Werf T S; Ligtenberg J J; Tulleken J E
CORPORATE SOURCE: Intensive and Respiratory Care Unit and Division of Immunology, Department of Internal Medicine, University Hospital Groningen, Groningen, The Netherlands..
j.w.fijen@int.azg.nl
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (2001 Apr) 124 (1) 16-20.
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614

AB Sepsis resulting in multiorgan failure and death is still a major problem in intensive care medicine, despite extensive attempts to interfere in the supposed underlying mechanism of a deranged immune system. This is not only due to the persistent lacunae in knowledge about the immune system in sepsis but also due to the lack of sufficient instruments for intervention. Inhibitors of the p38 mitogen-activated protein kinase (p38MAPK) have been used to study the signalling pathway of the immune response. In vitro and animal studies have demonstrated that blocking p38MAPK could mitigate the pro-inflammatory response and improve survival after endotoxaemia. Using an endotoxaemia model in healthy human volunteers we evaluated the attenuation of clinical and cytokine response to endotoxin after inhibition of p38MAPK by an oral dose of RWJ-67657, a pyrindinyl imidazole. We measured the clinical parameters temperature, blood pressure and heart rate. The proinflammatory cytokines tumour necrosis factor-alpha, interleukin-6 and interleukin-8 were measured by ELISA at various points during a 24-h period. Drug toxicity was evaluated by routine clinical and laboratory examinations. After a single dose dose of RWJ-67657 the temperature and blood pressure response remained at the basal level. The inhibition of TNF-alpha, IL-6 and IL-8 response was a dose dependent. With the maximum dosage, reduction in peak serum levels of the proinflammatory cytokines was greater than 90%. There was no drug-related toxicity. Interpretation: We conclude that inhibition of p38MAPK by RWJ-67657 might be a tool to intervene in the deranged immune response in sepsis and other inflammatory diseases.

L6 ANSWER 9 OF 43 MEDLINE
DUPLICATE 8
ACCESSION NUMBER: 2000255422 MEDLINE
DOCUMENT NUMBER: 20255422
PubMed ID: 10792949
TITLE: The effects of interleukin-10 in hemorrhagic shock.
AUTHOR: Karakozis S; Hinds M; Cook J W; Kim D; Provido H; Kirkpatrick J R
CORPORATE SOURCE: Department of Surgery, Washington Hospital Center, 110 Irving Street NW, Washington, DC 20010-2975, USA.
SOURCE: JOURNAL OF SURGICAL RESEARCH, (2000 May 15) 90 (2) 109-12.
Journal code: 0376340. ISSN: 0022-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000622
Last Updated on STN: 20000622
Entered Medline: 20000614
AB BACKGROUND: Interleukin-10 (IL-10) counteracts the effects of the proinflammatory cytokines interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF). Experimental data suggest that inhibition of these proinflammatory cytokines improves outcome in sepsis, endotoxemia, necrotizing pancreatitis, and other severe inflammatory states. We hypothesized that the administration of IL-10 would attenuate the release of proinflammatory cytokines after severe hemorrhagic shock. METHODS: To test our hypothesis, male Sprague-Dawley rats (N = 20) were divided into control and experimental groups. We induced hemorrhagic shock by removing a sufficient quantity of blood to maintain a mean arterial pressure of 50 mm Hg or less for 120 min. The animals were then resuscitated with shed blood and an equal volume of 0.9% saline. The experimental group received 10,000 units of IL-10 at the initiation of shock. Serum IL-1, IL-6, TNF, and lactate were

measured at baseline, after 120 min of shock, and 60 min after resuscitation. The rats were followed for 72 h to calculate survival. RESULTS: Similar levels of hypoperfusion were obtained in both groups as demonstrated by lactate levels and amount of shed blood. The survival rate (70%) was the same in both groups. Serum levels of IL-1 and IL-6 were not significantly different between the two groups, although there was a trend toward IL-6 suppression. TNF, however, was significantly lower in the IL-10-treated group at the end of shock (Wilcoxon test, P < 0. 025). CONCLUSION: Administration of IL-10 suppresses the TNF surge observed after severe hemorrhagic shock.

L6 ANSWER 10 OF 43 MEDLINE
DUPLICATE 9
ACCESSION NUMBER: 2000130974 MEDLINE
DOCUMENT NUMBER: 20130974
PubMed ID: 10663839
TITLE: Serum cytokine profile in reflux nephropathy.
AUTHOR: Jutley R S; Youngson G G; Eremin O; Ninan G K
CORPORATE SOURCE: Department of Surgery, University of Aberdeen Medical School, Foresterhill Hospital, Aberdeen, AB9 2ZG, UK.
SOURCE: PEDIATRIC SURGERY INTERNATIONAL, (2000) 16 (1-2) 64-8. Journal code: 8609169. ISSN: 0179-0358.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000307
AB Cytokines are small regulatory peptides with diverse functions. They regulate the immune system and modulate the inflammatory response, both of which are implicated in vesico-ureteric reflux (VUR) and associated reflux nephropathy (RN). The cytokine profile in VUR and RN has yet to be fully investigated. Blood was obtained from three subject groups immediately after induction of anaesthesia: group A [subjects with VUR and established RN, (N=9)]; group B [VUR alone but no associated RN, (N=6)]; and group C [age- and sex-matched controls with no history of urinary sepsis , (N=14)]. Serum cytokine levels of tumour-necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6), soluble TNF receptor-1 (sTNF-R1), and interleukin-8 (IL-8) were measured using standard ELISA technique. Serum levels of IL-6 were higher in group A subjects (1.798-4.638 pg/ml, median 3.253 pg/ml) than controls (1.531-2.078 pg/ml, median 1.798 pg/ml). There was no significant difference in levels in group B subjects (1.498-3. 048 pg/ml, median 1.948 pg/ml) and controls. These same relationships were observed for levels of TNF-alpha (group A: 8. 501-14.471 pg/ml, median 13.483 pg/ml; group B: 7.088-10.650 pg/ml, median 8.886 pg/ml; group C: 6.746-13.344 pg/ml, median 7.671 pg/ml) and sTNF-R1 (group A: 690.34-5780.74 pg/ml, median 1197.38 pg/ml; group B: 366.65-1401.62 pg/ml, median 592.82 pg/ml; C: 313.49-636.33 pg/ml, median 504.17 pg/ml). IL-8 was not significantly elevated in any of the study groups (A or B) compared with control group C (group A: 27.08-56.38 pg/ml, median 31.35 pg/ml; group B: 29.90-35. 87 pg/ml, median 31.35 pg/ml; group C: 25.05-30.22 pg/ml, median 29. 90 pg/ml). These results suggest there may be an immunological basis to RN.

L6 ANSWER 11 OF 43 MEDLINE
DUPLICATE 10
ACCESSION NUMBER: 2001326645 MEDLINE
DOCUMENT NUMBER: 21288463
PubMed ID: 11394228

TITLE: [Interleukin-6, procalcitonin, C-reactive protein and the immature to total neutrophil ratio (I/T) in the diagnosis of early-onset sepsis in low birth weight neonates].
Interleukin-6, prokalcitonin, C-reaktivni protein a pomer I/T v diagnostice casne sepse u novorozencu nizke porodni hmotnosti.
AUTHOR: Janota J; Stranak Z; Belohlavkova S
CORPORATE SOURCE: Ustav pro peci o matku a dite, Praha.
SOURCE: CESKA GYNEKOLOGIE, (2000 Dec) 65 Suppl 1 29-33.
Journal code: 9423768. ISSN: 1210-7832.
PUB. COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Czech
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705
AB OBJECTIVE: To determine the influence of early-onset neonatal sepsis on interleukin-6 (IL-6) and procalcitonin (PCT) levels in cord blood. To evaluate the significance of usually used infection markers--C-reactive protein (CRP) and immature to total neutrophil ratio (I/T)--and new markers (PCT, IL-6) for the diagnosis of early-onset neonatal sepsis. DESIGN: Prospective clinical study. SETTING: Institute for the Care of Mother and Child, Prague. METHODS: The serum levels of IL-6 and PCT were measured in cord blood in 37 low birht weight infants less than 35 week of gestation born in our institute. IL-6 and PCT levels were further evaluated together with CRP and I/T in neonatal blood within 2 hours after delivery. Neonatal sepsis within the first 72 hours of life was monitored. RESULTS: Differences in mean values of CRP, I/T, IL-6, and PCT between "sepsis proven" and "sepsis not proven" groups were not statistically significant. Only the difference between groups in cord blood PCT was of borderline significance (p = 0.06, higher in " sepsis proven" group). Fisher test showed significant dependence on sepsis in cord blood PCT only (cut-off point 0.4 ng/ml, p < or = 0.05). Other parameters did not show significant dependence on sepsis. Sensitivity for early onset sepsis above 50% was found in cord blood PCT only (sensitivity 60%, specificity 85.2%). PCT predictive accuracy for sepsis expressed as AUC value was 0.74 +/- 0.06. CONCLUSION: The only relatively sensitive marker and moderate predictor of early-onset sepsis in premature low birthweight infant was in our study cord blood PCT.

L6 ANSWER 12 OF 43 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 2000014237 MEDLINE
DOCUMENT NUMBER: 20014237
PubMed ID: 10548201
TITLE: Discrimination of infectious and noninfectious causes of early acute respiratory distress syndrome by procalcitonin.
COMMENT: Comment in: Crit Care Med. 1999 Oct;27(10):2304-5
AUTHOR: Brunkhorst F M; Eberhard O K; Brunkhorst R
CORPORATE SOURCE: Department of Intensive Care Medicine, Neukolln Teaching Hospital, Berlin, Germany.
SOURCE: CRITICAL CARE MEDICINE, (1999 Oct) 27 (10) 2172-6.
Journal code: 0355501. ISSN: 0090-3493.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111

Entered Medline: 19991116
AB OBJECTIVE: To test the sepsis marker procalcitonin (PCT) for its
applicability to discriminate between septic and nonseptic causes of acute
respiratory distress syndrome (ARDS). DESIGN: Prospective study, assessing
the course of PCT serum levels in early (within 72 hrs
after onset) ARDS. The three other inflammation markers neopterin,
interleukin-6 (IL-6), and C-reactive protein (CRP) were
tested in parallel. SETTING: Twenty-four-bed medical intensive care unit
of a 1,990-bed primary hospital, providing health care for an estimated
39,000 patients. PATIENTS: Twenty-seven patients, 18 male and nine female,
aged 16-85 yrs, with early ARDS of known cause (17 with septic and ten
with nonseptic ARDS) were enrolled in a prospective study between May 1994
and May 1995. INTERVENTIONS: Serum samples were drawn every 4-6 hrs for
measurement of PCT, neopterin, IL-6, and CRP concentrations. Blood
cultures, tracheal aspirates, and urine samples were obtained every 12-24
hrs. In 24 of 27 patients, bronchoscopic cultures were also obtained.
Clinical sepsis criteria as defined by the American College of
Chest Physicians/Society of Critical Care Medicine Consensus Conference
were checked daily. MEASUREMENTS AND MAIN RESULTS: Assessment of
inflammation marker serum levels in septic vs.
nonseptic ARDS. PCT serum levels were significantly
higher ($p < .0005$) in the patients with septic ARDS than in patients with
nonseptic ARDS within 72 hrs after onset of ARDS. There was no overlap
between the two groups. Also, neopterin allowed a differentiation ($p <$
.005), although a substantial overlap between serum
levels of septic and nonseptic patients was observed. No
discrimination could be achieved by determination of CRP and IL-6 levels.
CONCLUSION: PCT determination in early ARDS could help to discriminate
between septic and nonseptic underlying disease.

L6 ANSWER 13 OF 43 MEDLINE
DUPLICATE 12
ACCESSION NUMBER: 1999253575 MEDLINE
DOCUMENT NUMBER: 99253575
PubMed ID: 10321658
TITLE: Effects of ibuprofen on the physiology and survival of
hypothermic sepsis. Ibuprofen in Sepsis Study Group.
COMMENT: Comment in: Crit Care Med. 1999 Apr;27(4):669-70
AUTHOR: Arons M M; Wheeler A P; Bernard G R; Christman B W; Russell
J A; Schein R; Summer W R; Steinberg K P; Fulkerson W;
Wright P; Dupont W D; Swindell B B
CORPORATE SOURCE: Department of Medicine, Vanderbilt University School of
Medicine, Nashville, TN, USA.
CONTRACT NUMBER: HL 07123 (NHLBI)
HL 19153 (NHLBI)
HL 43167 (NHLBI)
SOURCE: CRITICAL CARE MEDICINE, (1999 Apr) 27 (4) 699-707.
Journal code: 0355501. ISSN: 0090-3493.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990526
AB OBJECTIVES: The objective was to compare the clinical and physiologic
characteristics of febrile septic patients with hypothermic septic
patients; and to examine plasma levels of cytokines tumor necrosis factor
alpha (TNF-alpha and interleukin 6 (IL-6) and the

lipid mediators thromboxane B2 (TxB2) and prostacyclin in hypothermic septic patients in comparison with febrile patients. Most importantly, we wanted to report the effect of ibuprofen treatment on vital signs, organ failure, and mortality in hypothermic sepsis. SETTING: The study was performed in the intensive care units (ICUs) of seven clinical centers in the United States and Canada. PATIENTS: Four hundred fifty-five patients admitted to the ICU who met defined criteria for severe sepsis and were suspected of having a serious infection. INTERVENTION: Ibuprofen at a dose of 10 mg/kg (maximum 800 mg) was administered intravenously over 30 to 60 mins every 6 hrs for eight doses vs. placebo (glycine buffer vehicle). MEASUREMENTS AND MAIN RESULTS: Forty-four (10%) septic patients met criteria for hypothermia and 409 were febrile. The mortality rate was significantly higher in hypothermic patients, 70% vs. 35% for febrile patients. At study entry, urinary metabolites of TxB2, prostacyclin, and serum levels of TNF-alpha and IL-6 were significantly elevated in hypothermic patients compared with febrile patients. In hypothermic patients treated with ibuprofen, there was a trend toward an increased number of days free of major organ system failures and a significant reduction in the 30-day mortality rate from 90% (18/20 placebo-treated patients) to 54% (13/24 ibuprofen-treated patients). CONCLUSIONS: Hypothermic sepsis has an incidence of approximately 10% and an untreated mortality twice that of severe sepsis presenting with fever. When compared with febrile patients, the hypothermic group has an amplified response with respect to cytokines TNF-alpha and IL-6 and lipid mediators TxB2 and prostacyclin. Treatment with ibuprofen may decrease mortality in this select group of septic patients.

L6 ANSWER 14 OF 43 MEDLINE
DUPLICATE 13
ACCESSION NUMBER: 1999426669
MEDLINE
DOCUMENT NUMBER: 99426669
PubMed ID: 10498355
TITLE: Dynamic profiles of interleukin-6 and the soluble form of CD25 in burned patients.
AUTHOR: Peteiro-Cartelle F J; Alvarez-Jorge A
CORPORATE SOURCE: Laboratories, Juan Canalejo Hospital, La Coruna, Spain.
SOURCE: BURNS, (1999 Sep) 25 (6) 487-91.
Journal code: 8913178. ISSN: 0305-4179.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991103
AB Changes in the time courses of serum levels of interleukin-6 (IL6) and the soluble form of CD25 (sCD25) were evaluated in 48 burned patients (31 had sepsis, 21 died). Differences among groups along the time were assessed with ANOVA. The Pearson's r correlation coefficient was used to relate quantitative variables. ROC curves were constructed to analyse the prognostic value of IL6 and sCD25. The values of IL6 and sCD25 were related to treatment outcome and time post-burn. In general, two patterns emerged: In non-survivors, there was a depression of sCD25 with time, and an increase in IL6 levels previous to death, whereas survivors had the opposite pattern. On admission, patients with higher levels of sCD25 had a bad prognosis.

L6 ANSWER 15 OF 43 MEDLINE
DUPLICATE 14
ACCESSION NUMBER: 1999223068
MEDLINE

DOCUMENT NUMBER: 99223068
PubMed ID: 10208387
TITLE: Changes in circulating levels of interleukin 6 in burned patients.
AUTHOR: Yeh F L; Lin W L; Shen H D; Fang R H
CORPORATE SOURCE: Department of Surgery, Veterans General Hospital-Taipei and National Yang-Ming University, Taiwan.
SOURCE: BURNS, (1999 Mar) 25 (2) 131-6.
Journal code: 8913178. ISSN: 0305-4179.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990607

AB Interleukin 6 (IL-6) levels in serial serum samples of 10 burned patients were analyzed. The total body surface areas (TBSA) of the burn injury varied from 30 to 85%. Among these 10 patients, five recovered and the other five, who were septic, expired. A significant difference in serum IL-6 values on admission (5-13 h postburn) was found ($p < 0.05$) between patients who survived or died from burn injury as analyzed by the Wilcoxon's rank sum test. In addition, a significant difference in serum IL-6 on admission was also found ($p < 0.05$) between patients with TBSA of greater or less than 50%. Afterwards, an initial peak serum IL-6 response was detected within 4 days postburn. Significant differences in the peak serum IL-6 levels were not found between patients with TBSA of greater or less than 50% and patients who survived or expired from burn injury. In the survivors, serum IL-6 remained low, while IL-6 increased markedly starting at about one to two weeks postburn in four of the five nonsurvivors with proven sepsis. Except for the patient who expired 42 days postburn, the maximum serum IL-6 values of the other four nonsurvivors were all greater than those of the five survivors from burn injury. Significant correlation ($p < 0.05$) relating the change in serum IL-6 and body temperature was observed in only two (one survivor and one nonsurvivor) of the ten patients. Changes in serum IL-6 were also compared with changes in circulating TNF-alpha and IL-8 determined previously. A similar pattern in the dynamic changes of circulating TNF-alpha, IL-8 and IL-6 was observed in the individual burned patient. An increase in serum levels of all three cytokines was detected postburn. Serum levels of three cytokines were significantly higher in the septic patients, who all died. It was considered that all three cytokines analyzed may play a significant role in the pathophysiology of sepsis in burned patients.

L6 ANSWER 16 OF 43 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 1998315686 MEDLINE
DOCUMENT NUMBER: 98315686
PubMed ID: 9618243
TITLE: Endotoxin and tumor necrosis factor alpha exert a similar proinflammatory effect in neonatal rat cardiomyocytes, but have different cardiodepressant profiles.
AUTHOR: Muller-Werdan U; Schumann H; Loppnow H; Fuchs R; Darmer D; Stadler J; Holtz J; Werdan K
CORPORATE SOURCE: Department of Medicine III, Klinikum Krollwitz, University of Halle-Wittenberg, Germany.
SOURCE: JOURNAL OF MOLECULAR AND CELLULAR CARDIOLOGY, (1998 May) 30 (5) 1027-36.
Journal code: 0262322. ISSN: 0022-2828.
PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980925
Last Updated on STN: 19980925
Entered Medline: 19980917

AB Bolus application of endotoxin to healthy volunteers results in reversible hemodynamic alterations, such as observed in septic cardiomyopathy. Currently, endotoxin-induced cardiodepression is mainly attributed to the endotoxin-induced release of proinflammatory cytokines into the circulation, particularly of tumor necrosis factor alpha and interleukin-1, the serum levels of these cytokines being enhanced in sepsis and septic shock, and also in various heart diseases. In this study, we report a proinflammatory effect of endotoxin (1-10 micrograms/ml, 24-h incubation period) on neonatal rat cardiomyocytes in serum-free culture, evidenced by induction of inducible nitric oxide synthase, enhanced release of nitrite (protein synthesis-dependent) and interleukin-6 into the supernatant, as well as an increase in cell-associated interleukin-1 and a specific cardiodepressant profile: endotoxin disrupts beta-adrenoceptor-mediated increase in pulsation amplitude, but alpha-adrenoceptor-induced increase in pulsation amplitude and arrhythmias are not suppressed. In the presence of dexamethasone (0.1 microM), the endotoxin-mediated blockade of beta-adrenergic responsiveness, as well as induction of inducible nitric oxide synthase, enhanced nitrite release and interleukin-1/-6-production are inhibited. In contrast, tumor necrosis factor alpha at a low concentration (10 U/ml) depresses alpha- and beta-adrenergic responsiveness in the presence of dexamethasone in a nitric oxide-independent manner. These data suggest a stimulatory effect of endotoxin on the cardiomyocyte and a specific proinflammatory and nitric oxide-dependent cardiodepressant profile of endotoxin.

L6 ANSWER 17 OF 43 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 1998260348 MEDLINE
DOCUMENT NUMBER: 98260348
PubMed ID: 9580629
TITLE: Modulation of mouse endotoxin shock by inhibition of phosphatidylcholine-specific phospholipase C.
AUTHOR: Tschaikowsky K; Schmidt J; Meisner M
CORPORATE SOURCE: Department of Anesthesiology, University of Erlangen-Nurnberg, Germany.. klaus.tschaikowsky@rzmail.uni-erlangen.de
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1998 May) 285 (2) 800-4.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980618
Last Updated on STN: 19990129
Entered Medline: 19980608

AB During Gram-negative bacterial infections, lipopolysaccharide (LPS) interacts with monocyte/macrophage receptors, resulting in a host defense response. Activation of intracellular signal transduction pathways implicating various protein kinase and phospholipases is crucial in activating the transcription of genes encoding proinflammatory cytokines and inducible nitric oxide synthase (iNOS). In this article, we demonstrate that in mouse, endotoxin shock activation of

phosphatidylcholine-specific phospholipase C (PC-PLC) plays a major role in controlling the inflammatory response. Inhibition of PC-PLC by the specific inhibitor tricyclodecan-9-yl-xanthogenate (D609) before LPS reduced the release of interleukin-1 beta, interleukin-6 and nitric oxide (NO) in vivo. In contrast, tumor necrosis factor-alpha serum levels were not altered by the pretreatment with D609. Consequently, survival from endotoxin shock of D609-treated animals was significantly improved compared with control animals (45% vs. 20%). Thus, inhibition of PC-PLC can reduce the inflammatory response to LPS and may serve as a novel approach to therapy of sepsis.

L6 ANSWER 18 OF 43 MEDLINE
DUPLICATE 17
ACCESSION NUMBER: 1999068697 MEDLINE
DOCUMENT NUMBER: 99068697
PubMed ID: 9853808
TITLE: Validation of an automated enzyme immunoassay for Interleukin-6 for routine clinical use.
AUTHOR: Fraunberger P; Pfeiffer M; Cremer P; Holler E; Nagel D; Dehart I; Thein M; Walli A K; Seidel D
CORPORATE SOURCE: Institut fur Klinische Chemie, Klinikum Grosshadern, LMU Munchen, Munich, Germany.
SOURCE: CLINICAL CHEMISTRY AND LABORATORY MEDICINE, (1998 Oct) 36 (10) 797-801.
Journal code: 9806306. ISSN: 1434-6621.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990301
Last Updated on STN: 19990301
Entered Medline: 19990212
AB Serum levels of Interleukin-6 (IL-6), a proinflammatory cytokine, are increased in early stages of inflammatory diseases such as infection and sepsis. Assay systems which permit its measurement within a few hours and as a single measurement have not been reported so far. We therefore evaluated a now commercially available automated method for IL-6 measurement on the Cobas Core immunological analyzer (Roche Diagnostic Systems) which enables single IL-6 measurement within about 1 hour. The automated assay correlates well with an established, manual microtiter plate assay (Biosource GmbH) which uses the same antibodies and reagents (r=0.98). Accuracy of the automated method was established by adding known amounts of IL-6 international reference preparation. Recovery of the international standard was in the range of 92104%. The automated assay had a precision of singletons below 6% and was linear up to 2800 pg/ml. This automated assay provides a suitable, convenient and time saving method for measurement of IL-6 serum levels in the routine clinical laboratory.

L6 ANSWER 19 OF 43 CAPLUS
COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:69548 CAPLUS
DOCUMENT NUMBER: 128:152980
TITLE: The dual role of interferon-.gamma. in experimental Staphylococcus aureus septicemia versus arthritis
AUTHOR(S): Zhao, Y.-X.; Nilsson, I.-M.; Tarkowski, A.
CORPORATE SOURCE: Departments Rheumatology Clinical Immunology, University Goteborg, Goteborg, Swed.
SOURCE: Immunology (1998), 93(1), 80-85
CODEN: IMMUAM; ISSN: 0019-2805

PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To evaluate the role of interferon-.gamma. (IFN-.gamma.) in Staphylococcus aureus infection, the authors investigated the effects of supplementation with and neutralization of IFN-.gamma. during septicemia and arthritis in a murine model. In vivo administration of IFN-.gamma. both before and after bacterial inoculation significantly decreased mortality on one hand but enhanced the development of arthritis on the other. Treatment of mice with anti-IFN-.gamma. monoclonal antibodies (mAb) before and after bacterial inoculation did not significantly influence the survival rate but decreased the frequency and severity of arthritis. The beneficial effect of supplementation with IFN-.gamma. on septicemia was correlated to the increased phagocytosis and bacterial clearance from liver and kidneys. The down-regulation of the development of arthritis by anti-IFN-.gamma. mAb was accompanied by the decreased serum tumor necrosis factor .alpha., interleukin-6 and interleukin-1.beta. levels. These results demonstrate a significant role for IFN-.gamma. in simultaneous protection against septicemia but promotion for the development of septic arthritis.

L6 ANSWER 20 OF 43 MEDLINE
DUPLICATE 18
ACCESSION NUMBER: 97413373 MEDLINE
DOCUMENT NUMBER: 97413373
PubMed ID: 9269788
TITLE: Downregulation of the proinflammatory cytokine response to endotoxin by pretreatment with the nontoxic lipid A analog SDZ MRL 953 in cancer patients.
AUTHOR: Kiani A; Tschiersch A; Gaboriau E; Otto F; Seiz A; Knopf H P; Stutz P; Farber L; Haus U; Galanos C; Mertelsmann R; Engelhardt R
CORPORATE SOURCE: Department of Internal Medicine I, University Hospital of Freiburg, Germany.
SOURCE: BLOOD, (1997 Aug 15) 90 (4) 1673-83.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971008
Last Updated on STN: 19971008
Entered Medline: 19970924
AB Interfering with the endotoxin-mediated cytokine cascade is thought to be a promising approach to prevent septic complications in gram-negative infections. The synthetic lipid A analog SDZ MRL 953 has been shown to be protective against endotoxic shock and bacterial infection in preclinical in vivo models. As part of a trial of unspecific immunostimulation in cancer patients, we conducted a double-blind, randomized, vehicle-controlled phase I trial of SDZ MRL 953 to investigate, first, its biologic effects and safety of administration in humans and, second, its influence on reactions to a subsequent challenge of endotoxin (Salmonella abortus equi). Twenty patients were treated intravenously with escalating doses of SDZ MRL 953 or vehicle control, followed by an intravenous application of endotoxin (2 ng/kg of body weight [BW]). Administration of SDZ MRL 953 was safe and well-tolerated. SDZ MRL 953 itself increased granulocyte counts and serum levels of granulocyte colony-stimulating factor (G-CSF) and interleukin-6 (IL-6), but not of the proinflammatory cytokines tumor necrosis factor-alpha (TNF-alpha), IL-1beta, and IL-8. Compared with vehicle

control, pretreatment with SDZ MRL 953 markedly reduced the release of TNF-alpha, IL-1beta, IL-8, IL-6, and G-CSF, but augmented the increase in granulocyte counts to endotoxin. Induction of tolerance to the endotoxin-mediated cascade of proinflammatory cytokines by pretreatment with SDZ MRL 953 in patients at risk may help to prevent complications of gram-negative sepsis.

L6 ANSWER 21 OF 43 MEDLINE
DUPLICATE 19
ACCESSION NUMBER: 1998010367 MEDLINE
DOCUMENT NUMBER: 98010367
PubMed ID: 9350884
TITLE: Interleukin 6, but not tumour necrosis factor-alpha, is a good predictor of severe infection in febrile neutropenic and non-neutropenic children with malignancy.
AUTHOR: Abrahamsson J; Pahlman M; Mellander L
CORPORATE SOURCE: Department of Pediatrics, University of Goteborg, Sweden.
SOURCE: ACTA PAEDIATRICA, (1997 Oct) 86 (10) 1059-64.
Journal code: 9205968. ISSN: 0803-5253.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971119
AB OBJECTIVE: Interleukin-6 (IL6), tumor necrosis factor-alpha (TNF-alpha) and interferon-gamma (IFN-gamma) are important mediators of the inflammatory response in human infection. The aim of this study was to determine the relationship between serum levels of IL6, TNF-alpha, IFN-gamma and CRP in febrile children with malignant disease, and relate these levels to aetiology of fever, presence of neutropenia and the effect of untreated malignancy. METHODS: 110 febrile episodes in 70 children with malignant disease were included. Cytokine analyses were performed with sensitive immunoradiometric methods using double monoclonal antibodies. RESULTS: IL6 had a sensitivity of 74% in detecting sepsis in children with fever and malignant disease. This sensitivity was not influenced by the presence of neutropenia or newly diagnosed malignancy. A positive correlation between IL6 and the CRP levels on the following day was observed (r = .53). TNF-alpha was elevated in 22% of the episodes and mean levels were significantly higher in untreated malignancy but lower in neutropenic patients. IFN-gamma was elevated in 18% of cases and correlated strongly with mean TNF-alpha levels. CONCLUSIONS: IL6 is a sensitive and early predictor of bacterial infection in both neutropenic and non-neutropenic febrile children with malignancy. It is more sensitive than CRP in detecting sepsis, but the predictive value is too low to allow IL6 levels to influence initial treatment decisions in patients with granulocytopenia. TNF-alpha production seems to be impaired in neutropenic children and serum TNF-alpha cannot be employed as an indicator of bacterial infection.

L6 ANSWER 22 OF 43 MEDLINE
DUPLICATE 20
ACCESSION NUMBER: 97276938 MEDLINE
DOCUMENT NUMBER: 97276938
PubMed ID: 9130631
TITLE: Superantigen and endotoxin synergize in the induction of lethal shock.
AUTHOR: Blank C; Luz A; Bendigs S; Erdmann A; Wagner H; Heeg K
CORPORATE SOURCE: Institute of Medical Microbiology, Immunology and Hygiene, Munich, Germany.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Apr) 27 (4) 825-33.

Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970602
Last Updated on STN: 19970602
Entered Medline: 19970522

AB Endotoxin (lipopolysaccharide; LPS) and superantigens (exotoxins) have been identified as potent inducers of lethal shock. While endotoxin primarily interacts with CD14 receptors on macrophages, superantigens like the staphylococcal enterotoxin B (SEB) preferentially activate T cells. Both cell types are triggered to release pro-inflammatory cytokines that in turn induce lethal shock. We analyzed whether endotoxin and superantigen interact during the induction phase of lethal shock. We report that LPS and SEB operate synergistically. Lethal doses of both inducers were reduced 100-fold when given in combination. The induced serum levels of tumor necrosis factor, interleukin-6, and interferon-gamma (IFN-gamma) were elevated and remained high for a prolonged period. Moreover, synergistic action of LPS and SEB induced lethal toxic shock even without presensitization of mice with D-galactosamine (D-GalN). Opposed to D-GalN-pretreated mice, mice injected with LPS and SEB showed less liver damage, but rather apoptosis of epithelial cells in the bowel. Cyclosporin A and treatment with anti-IFN-gamma monoclonal antibody blocked the synergistic action of LPS and SEB, indicating that T cell-derived IFN-gamma is the mediator of the observed synergism. Concomitant injection of LPS and SEB had no influence on SEB-induced T cell deletion and anergy induction. Since Gram-positive and Gram-negative bacteria can be recovered from septic blood samples, the synergistic action of endotoxin and superantigens might be relevant during lethal septicemia.

L6 ANSWER 23 OF 43 CAPLUS
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ACCESSION NUMBER: 1997:621821 CAPLUS
DOCUMENT NUMBER: 127:276994
TITLE: Immunological status of septic and trauma patients. I. High tumor necrosis factor .alpha. serum levels in septic and trauma patients are not responsible for increased mortality; a prognostic value of serum interleukin 6
AUTHOR(S): Adamik, Barbara; Zimecki, Michal; Wlaszczyk, Andrzej; Kubler, Andrzej
CORPORATE SOURCE: Department of Anesthesiology and Intensive Therapy, University Medical School, Wroclaw, 50-368, Pol.
SOURCE: Archivum Immunologiae et Therapiae Experimentalis (1997), 45(2-3), 169-175
CODEN: AITEAT; ISSN: 0004-069X
PUBLISHER: Zaklad Narodowy imienia Ossolinskich
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to monitor plasma interleukin 6 (IL-6), and tumor necrosis factor .alpha. (TNF-.alpha.), levels in patients with sepsis, septic shock and multiple organ dysfunction syndrome admitted to the intensive care unit. The patients obtained adequate supportive therapy. Plasma samples were taken upon admission, then on days 1, 2, and 5 following admission. IL-6 and TNF-.alpha. levels were detd. using bioassays (7TD1 and WEHI-164.13 indicator cell lines, resp.). The results showed that the kinetics of the cytokine release in septic patients differed significantly between survivors and non-survivors. In survivors IL-6 concns. were initially high, fell down rapidly on day 1 after

admission, and persisted very low throughout the monitoring time. In contrast, relatively low IL-6 levels in the non-survivors, registered upon admission, rose significantly with peak values on day 3 of observation, declining thereafter. TNF-.alpha. levels were initially higher in survivors than in non-survivors, declined on day 1 following admission, and on day 5 they were higher than the initial values. In non-survivors, the starting concns. of TNF-.alpha. were much lower than in survivors with a peak on day 3 with a tendency to fall on day 7. The profiles of cytokine prodn. by traumatic patients (90% survivors) revealed low and progressively diminishing levels of IL-6, contrasting with constantly increasing concns. of TNF-.alpha. within the monitoring period. The authors conclude that high IL-6 levels in septic patients accompanied by high TNF-.alpha. levels may indicate bad prognosis. In contrast, rapidly diminishing serum IL-6 levels, even in the presence of high TNF-.alpha. levels, could indicate a very good chance for survival. Similar conclusion can be drawn from the monitoring of cytokine prodn. in traumatic, non-septic patients since almost all of them recovered. The authors also speculate that TNF-.alpha. presence in circulating blood is essential for regeneration of tissues and wound healing.

L6 ANSWER 24 OF 43 MEDLINE
DUPLICATE 21
ACCESSION NUMBER: 97211299 MEDLINE
DOCUMENT NUMBER: 97211299
PubMed ID: 9058297
TITLE: Hepatocyte growth factor in assessment of acute pancreatitis: comparison with C-reactive protein and interleukin-6.
AUTHOR: Ueda T; Takeyama Y; Hori Y; Nishikawa J; Yamamoto M; Saitoh Y
CORPORATE SOURCE: First Department of Surgery, Kobe University School of Medicine, Japan.

SOURCE: JOURNAL OF GASTROENTEROLOGY, (1997 Feb) 32 (1) 63-70.
Journal code: 9430794. ISSN: 0944-1174.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970609
Last Updated on STN: 19970609
Entered Medline: 19970523

AB Serum levels of hepatocyte growth factor (HGF), C-reactive protein (CRP), and interleukin-6 (IL-6) were determined at the time of admission in 38 patients with acute pancreatitis. The clinical utility of HGF for the detection of severe pancreatitis and for predicting prognosis, bacterial infection (infected pancreatic necrosis or sepsis), and organ dysfunction (liver, kidney, and lung) during the clinical course of acute pancreatitis was compared with the clinical utility of CRP and IL-6 by analysis of receiver operator characteristic (ROC) curves. The optimum cutoff levels of HGF for severity, prognosis, infection, hepatic dysfunction, renal dysfunction, and respiratory dysfunction were 0.9, 1.1, 1.0, 1.1, 1.1, and 1.0 ng/ml, respectively. HGF was as useful as CRP and more useful than IL-6 for detection of severe pancreatitis and for predicting hepatic dysfunction. Moreover, HGF was more useful than CRP or IL-6 for predicting prognosis, renal dysfunction, and respiratory dysfunction. However, for predicting infection, CRP was more useful than HGF. These results suggest that serum HGF levels on admission may be a useful new clinical parameter for determining the prognosis of acute pancreatitis and that HGF may be closely related to the organ dysfunction of acute pancreatitis.

L6 ANSWER 25 OF 43 MEDLINE
DUPLICATE 22
ACCESSION NUMBER: 97066033
MEDLINE
DOCUMENT NUMBER: 97066033
PubMed ID: 8909514
TITLE: High tumor necrosis factor serum level is associated with increased survival in patients with abdominal septic shock: a prospective study in 59 patients.
AUTHOR: Riche F; Panis Y; Laisne M J; Briard C; Cholley B; Bernard-Poenaru O; Graulet A M; Gueris J; Valleur P
CORPORATE SOURCE: Department of Anesthesiology, Lariboisiere Hospital, Paris, France.
SOURCE: SURGERY, (1996 Nov) 120 (5) 801-7.
Journal code: 0417347. ISSN: 0039-6060.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961213
AB BACKGROUND: In several studies including patients with septic shock of various origins, high serum cytokine levels have been reported to correlate with poor outcome. The aim of this prospective study was to assess the prognostic value of cytokine serum levels in a group of patients with perioperative septic shock of digestive origin. METHODS: From January 1992 to December 1994, 59 patients were evaluated (mean age, 68 +/- 15 years). From the first day of septic shock to day 7, blood was drawn every day to measure the conventional biologic parameters (white blood cell count, platelet count, hematocrit, blood urea nitrogen level, serum electrolytes level, pH, blood gases, serum lactate level, coagulation parameters, liver function tests) and tumor necrosis factor (TNF), interleukin-1, and interleukin-6. RESULTS: No difference was observed between the 26 survivors and the 33 nonsurvivors with regard to age, gender, and cause of sepsis. On admission, mean platelet count was significantly higher in the survivors than in the nonsurvivors (260 +/- 142 versus 177 +/- 122 10(9)/L; p = 0.01). Mean blood urea nitrogen level was significantly lower in the survivors than in the nonsurvivors (9.6 +/- 9 versus 12 +/- 7 mmol/L; p = 0.04). No difference was observed between survivors and nonsurvivors for the other conventional biologic parameters and for serum interleukin-1 and interleukin-6 levels. Mean serum TNF level tended to be higher in survivors than in nonsurvivors (565 +/- 1325 versus 94 +/- 69 pg/ml; not significant). In the group survivor 9 (35%) of 26 patients had a serum TNF level greater than 200 pg/ml versus 2 (6%) of 33 patients in the nonsurvivor group ($p < 0.02$). Survival was noted in 6 (100%) of 6 patients who had both a serum TNF level greater than 200 pg/ml and a platelet count greater than 100.10(9)/L versus 1 (11%) of 9 in patients with neither of these criteria ($p < 0.01$). CONCLUSIONS: In our patients with abdominal septic shock, high serum TNF levels were associated with increased survival. The high serum level of TNF may reflect the efficacy of peritoneal inflammatory response against abdominal sepsis. Although this possibility must be further explored, a score combining the serum TNF level and platelet count could be helpful for the prognostic assessment of patients with abdominal septic shock.

L6 ANSWER 26 OF 43 MEDLINE
DUPLICATE 23
ACCESSION NUMBER: 96304180
MEDLINE
DOCUMENT NUMBER: 96304180
PubMed ID: 8753088

PATENT NO. KIND DATE APPLICATION NO. DATE

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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
DE 4409513 C1 19951019 DE 1994-4409513 19940319
IL 112427 A1 19981206 IL 1995-112427 19950124
CA 2182723 AA 19950810 CA 1995-2182723 19950127
AU 9515201 A1 19950821 AU 1995-15201 19950127
CN 1140414 A 19970115 CN 1995-191517 19950127
JP 09509411 T2 19970922 JP 1995-520363 19950127
BR 9506741 A 19971021 BR 1995-6741 19950127
EP 804236 A1 19971105 EP 1995-906353 19950127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI
HU 76875 A2 19971229 HU 1996-2169 19950127
TW 403656 B 20000901 TW 1995-84100744 19950127
CZ 290843 B6 20021016 CZ 1996-2322 19950127
ZA 9500956 A 19951011 ZA 1995-956 19950207
FI 9603101 A 19960806 FI 1996-3101 19960806
NO 9603280 A 19961004 NO 1996-3280 19960806
MX 9603243 A 20000228 MX 1996-3243 19960807
US 6235281 B1 20010522 US 1996-687328 19960807
AU 9915495 A1 19990401 AU 1999-15495 19990208
US 2001010819 A1 20010802 US 2001-782290 20010214
PRIORITY APPLN. INFO.: DE 1994-4403669 A 19940207
DE 1994-4409513 A 19940319
AU 1995-15201 A3 19950127
WO 1995-EP291 W 19950127
US 1996-687328 A1 19960807

AB Tumor necrosis factor (TNF) antagonists, esp. anti-TNF antibodies and their fragments, are useful in prodn. of drugs to treat diseases characterized by elevated interleukin-6 serum levels, e.g. sepsis.

L6 ANSWER 30 OF 43 MEDLINE DUPLICATE 26
ACCESSION NUMBER: 96108305 MEDLINE
DOCUMENT NUMBER: 96108305
PubMed ID: 8658074
TITLE: High IL-6 serum levels are associated with septic shock and mortality in septic patients with severe leukopenia due to hematological malignancies.
AUTHOR: Antonelli M; Raponi G M; Martino P; Rosa G; Conti G; Jalouk J; Gasparetto A
CORPORATE SOURCE: Institute of Anesthesiology and Intensive Care, La Sapienza University of Rome, Italy.
SOURCE: SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES, (1995) 27 (4) 381-4.
Journal code: 0215333. ISSN: 0036-5548.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960808
Last Updated on STN: 19980206
Entered Medline: 19960731

AB The serum levels of immunoreactive interleukin -6 (IL-6) and tumor necrosis factor (TNF) were analyzed in 14 leukopenic patients with documented sepsis, at 60 min (T0), 24 h (T1), and one week (T3) after the onset of sepsis syndrome. Sera

from 10 leukopenic patients without sepsis (controls) were also
tested. All septic patients had high IL-6 levels at T0. These levels
persisted only in the seven patients who died of septic shock, presenting
a 30-fold increase ($p<0.001$) as compared to the survivors and the
controls. At T3, 7 survivors had recovered from sepsis and
showed low IL-6 serum levels. The TNF serum
concentration always <30 pg/ml in both the subjects and in the controls.
The C-reactive protein (CRP) and clinical parameters appeared to be less
specifically associated with shock and mortality than IL-6.

L6 ANSWER 31 OF 43 MEDLINE
DUPLICATE 27
ACCESSION NUMBER: 95271638 MEDLINE
DOCUMENT NUMBER: 95271638
PubMed ID: 7752214
TITLE: Cytokine stimulation during Salmonella typhimurium sepsis
in Itys mice.
AUTHOR: Jotwani R; Tanaka Y; Watanabe K; Tanaka K; Kato N; Ueno K
CORPORATE SOURCE: Institute of Anaerobic Bacteriology, Gifu University School
of Medicine, Japan.
SOURCE: JOURNAL OF MEDICAL MICROBIOLOGY, (1995 May) 42 (5) 348-52.
Journal code: 0224131. ISSN: 0022-2615.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950629
Last Updated on STN: 19950629
Entered Medline: 19950622
AB Cytokine production was measured in mice during Salmonella typhimurium
sepsis and intoxication. In mice given live S. typhimurium (10
cfu/mouse), by intra-peritoneal injection, serum levels
of tumour necrosis factor (TNF)-alpha and interleukin-6
increased steadily from day 1 until day 4. Interferon-gamma levels showed
a transient peak on day 3. Interleukin-1-alpha levels were very low. There
were high bacterial counts in the livers at day 3 and deaths occurred from
day 4 onwards. Intraperitoneal injection of lipopolysaccharide or
heat-killed bacteria also induced all of the cytokines, but their time of
appearance and levels varied greatly. Cytokine induction by heat-killed
bacteria was more marked. Endotoxaemia decreased with time during
intoxication and increased during sepsis. Bioactive TNF, as
measured by a cytotoxicity assay, was found only in mice given heat-killed
bacteria.

L6 ANSWER 32 OF 43 MEDLINE
DUPLICATE 28
ACCESSION NUMBER: 95109670 MEDLINE
DOCUMENT NUMBER: 95109670
PubMed ID: 7810656
TITLE: Interleukin-6 inhibits hepatocyte taurocholate uptake and
sodium-potassium-adenosinetriphosphatase activity.
AUTHOR: Green R M; Whiting J F; Rosenbluth A B; Beier D; Gollan J L
CORPORATE SOURCE: Division of Gastroenterology, Brockton/West Roxbury
Veterans Affairs Medical Center, Boston, Massachusetts.
CONTRACT NUMBER: DK-07533 (NIDDK)
DK-36887 (NIDDK)
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1994 Dec) 267 (6 Pt 1) G1094-100.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 19950215

Last Updated on STN: 19950215
Entered Medline: 19950131

AB The potential effects of cytokines on hepatocellular transport functions remain undefined. Interleukin-6 (IL-6) is a cytokine that is produced in sepsis, hepatitis, and other inflammatory conditions often associated with cholestasis. Using cultured rat hepatocytes, we have investigated the effects of IL-6 on hepatocellular bile salt uptake. Because hepatocyte Na(+)-K(+)-adenosinetriphosphatase (ATPase) produces the electrochemical gradient that drives sodium-dependent bile salt contransport, we also examined the effects of IL-6 on Na(+)-K(+)-ATPase activity. Hepatocytes cultured for 20 h in media containing IL-6 exhibited a dose-dependent noncompetitive inhibition of [3H]taurocholate uptake, which was maximal at an IL-6 dose of 100 U/ml. IL-6 treatment had no effect on hepatocyte sodium-independent taurocholate uptake. Northern blotting of RNA from cultured hepatocytes revealed that IL-6 had no effect on steady-state RNA levels of the Na(+)-taurocholate transporter (Ntcp). Hepatocytes incubated with IL-6 for 20 h, however, exhibited a 55% decrease in hepatocyte Na(+)-K(+)-ATPase activity. This effect also was dose dependent, with maximal inhibition occurring at an IL-6 dose of 100 U/ml. Similar treatment with IL-6 did not influence hepatocyte Mg(2+)-ATPase activity. The inhibition of Na(+)-K(+)-ATPase activity induced by IL-6 provides a putative mechanism for the observed inhibition of sodium-dependent taurocholate uptake. Since modulation of bile salt transport and Na(+)-K(+)-ATPase activity occurred at IL-6 concentrations comparable to the serum levels observed in patients with severe inflammatory states, these findings have potential pathophysiological relevance for the cholestasis of sepsis and other inflammatory disorders.

L6 ANSWER 33 OF 43 CAPLUS
COPYRIGHT 2003 ACS DUPLICATE 29
ACCESSION NUMBER: 1995:474676 CAPLUS
DOCUMENT NUMBER: 122:237432
TITLE: Kinetics of serum levels of interleukin-6 in Staphylococcus aureus septicemia
AUTHOR(S): Soederqist, B.; Sundqvist, K. -G.; Vikerfors, T.
CORPORATE SOURCE: Department Infectious Diseases, Orebro Medical Center Hospital, Orebro, S-70185, Swed.
SOURCE: Zentralblatt fuer Bakteriologie, Supplement (1994), 26, 446-8
CODEN: ZBASE2; ISSN: 0941-018X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The kinetics of interleukin-6 (IL-6) serum concns. were analyzed in patients with a culture verified S. aureus septicemia. All patients had elevated IL-6 serum concns. on admission. In most cases a subsequent rapid decrease to low levels was registered within 10 days. In most cases changes in IL-6 serum concns. reflected the clin. course. The raised IL-6 levels were concomitant with increases in other inflammatory parameters and a relation was found between IL-6 serum concns. and levels of C-reactive protein.

L6 ANSWER 34 OF 43 MEDLINE DUPLICATE 30
ACCESSION NUMBER: 95261963 MEDLINE
DOCUMENT NUMBER: 95261963
PubMed ID: 7743368
TITLE: Serum levels of end products of nitric oxide synthesis correlate positively with tumor necrosis factor alpha and negatively with body temperature in patients with postoperative abdominal sepsis.
AUTHOR: Barthlen W; Stadler J; Lehn N L; Miethke T; Bartels H; Siewert J R

CORPORATE SOURCE: Department of Surgery, Technical University, Munich, Germany.
SOURCE: SHOCK, (1994 Dec) 2 (6) 398-401.
Journal code: 9421564. ISSN: 1073-2322.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL) (CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950621
Last Updated on STN: 19950621
Entered Medline: 19950614
AB Nitric oxide (NO) has been implicated as the principal mediator of the catecholamine resistant vasodilation in septic shock. In this pilot study, we wanted to know if the serum values of nitrite/nitrate (NO2/NO3), the stable endproducts of NO biosynthesis, are elevated in patients with septic shock. Furthermore, we investigated whether there is a correlation between NO2/NO3 serum levels and tumor necrosis factor alpha or interleukin 6. NO2/NO3 serum values were significantly elevated in septic patients compared to controls (72.1 +/- 6.1 vs. 35.7 +/- 9.2 microM, $p < .001$). There was a significant positive correlation between serum values of NO2/NO3 and tumor necrosis factor alpha ($rs = 0.59$, $p < .001$). In contrast, no correlation between NO2/NO3 and interleukin 6 was found. With the exception of body core temperature, which showed a negative correlation with NO2/NO3 levels, no clinical variable turned out to be significantly related to NO biosynthesis. These data indicate a potential role for NO in the clinical course of abdominal sepsis, but points out that more specific data has to be evaluated by prospective clinical studies in order to understand the complex pathophysiologic role of this novel mediator.

L6 ANSWER 35 OF 43 MEDLINE
DUPLICATE 31
ACCESSION NUMBER: 95025111 MEDLINE
DOCUMENT NUMBER: 95025111
PubMed ID: 7938903
TITLE: Blood cytokine and complement levels in patients with sepsis.
AUTHOR: Takakuwa T; Endo S; Nakae H; Kikuchi M; Baba N; Inada K; Yoshida M
CORPORATE SOURCE: Critical Care and Emergency Center, Iwate Medical University, Morioka, Japan.
SOURCE: RESEARCH COMMUNICATIONS IN CHEMICAL PATHOLOGY AND PHARMACOLOGY, (1994 Jun) 84 (3) 291-300.
Journal code: 0244734. ISSN: 0034-5164.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941101
AB We measured serum levels of endotoxin, cytokines, and eicosanoids and investigated their relationship to serum complement levels in patients with sepsis. Serum endotoxin (Et) levels (5.3 +/- 2.4 pg/ml) were within the normal range, but levels of tumor necrosis factor-alpha (TNF-alpha, 114 +/- 104.94 pg/ml), interleukin 6 (IL-6, 86.7 +/- 50.9 pg/ml), interleukin 8 (IL-8, 86.8 +/- 49.7 pg/ml), type-II phospholipase A2 (type II PLA2, 211.3 +/- 193.9 ng/ml), leukotriene B4 (LTB4, 88.7 +/- 27.2 pg/ml), thromboxane B2 (TXB2, 58.7 +/- 50.9 pg/ml) and 6-keto-prostaglandin F1 alpha (PGF1 alpha, 21.0 +/- 11.0 pg/ml) levels were above normal. Levels of C3a (1088.4 +/- 83.8.7 ng/ml)

and C4a (1951.5 +/- 1697.8 ng/ml) were also above normal; C3 (66.0 +/-
25.6 mg/dl) and C4 (23.6 +/- 5.3 mg/dl) were within the normal range, and
C5a was lower than the detectable limit in all but one of the subjects.
Serum TNF-alpha was significantly correlated with C3a ($p < 0.001$). Serum
IL-6 had a significant negative correlation with C3 ($p = 0.002$) and C4 (p
= 0.010). Type II PLA2 was significantly correlated with C3a ($p < 0.001$).
There were no significant correlations between serum Et or IL-8 and serum
C3, C4, C3a or C4a. Our findings suggest that increased levels of
TNF-alpha, IL-6, and Type II PLA/ in patients with sepsis
contribute to activation of the complement system.

L6 ANSWER 36 OF 43 MEDLINE
DUPLICATE 32
ACCESSION NUMBER: 95253988 MEDLINE
DOCUMENT NUMBER: 95253988
PubMed ID: 7735958
TITLE: Changes in skeletal muscle pO2 after administration of
anti-TNF alpha-antibody in patients with severe
sepsis: comparison to interleukin-
6 serum levels, APACHE II, and Elebute scores.
AUTHOR: Boekstegers P; Weidenhofer S; Zell R; Holler E; Kapsner T;
Redl H; Schlag G; Kaul M; Kempeni J; Werdan K
CORPORATE SOURCE: Department of Internal Medicine I, Klinikum Grosshadern,
University of Munich, Germany.
SOURCE: SHOCK, (1994 Apr) 1 (4) 246-53.
Journal code: 9421564. ISSN: 1073-2322.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950615
Last Updated on STN: 19950615
Entered Medline: 19950607
AB In 20 patients with severe sepsis, skeletal muscle pO2 was
continuously measured in order to assess whether a decrease of skeletal
muscle pO2 was accompanied by an improvement of sepsis after
repeated administration of F(ab')2 fragments of a murine anti-TNF
alpha-antibody. Abnormally high skeletal muscle pO2 decreased from 43.5
+/- 10.9 mmHg (day 0) to 36.4 +/- 10.1 mmHg within 24 h after the first
administration of anti-TNF alpha-antibody (day 1, $p = .006$, $n = 20$) and
remained at 34.6 +/- 7.7 mmHg thereafter (mean day 2-7, $p = .004$). The
decrease of skeletal muscle pO2 within 24 h exceeded 5 mmHg (-7 to -19
mmHg) in 11 patients in contrast to nine patients (-4 to +4 mmHg). Only in
the patients showing a decrease of skeletal muscle pO2 did sepsis
improve as determined by Elebute score, APACHE II score, and
interleukin-6 serum levels. The
change of skeletal muscle pO2 within 24 h was associated with a change of
interleukin-6 serum levels within 24
h ($r = .5$, $n = 20$), with a change of Elebute score ($r = .7$, $n = 20$) and of
APACHE II score ($r = .62$). These data suggest that a decrease of skeletal
muscle pO2 might be an early indicator of improvement of sepsis
after administration of anti-TNF alpha-antibodies.

L6 ANSWER 37 OF 43 MEDLINE
DUPLICATE 33
ACCESSION NUMBER: 93056706 MEDLINE
DOCUMENT NUMBER: 93056706
PubMed ID: 1431255
TITLE: Effectiveness of a human monoclonal anti-endotoxin antibody
(HA-1A) in gram-negative sepsis: relationship to endotoxin
and cytokine levels.
COMMENT: Comment in: J Infect Dis. 1993 Jul;168(1):246-8
AUTHOR: Wortel C H; von der Mohlen M A; van Deventer S J; Sprung C

L; Jastremski M; Lubbers M J; Smith C R; Allen I E; ten Cate J W
CORPORATE SOURCE: Department of Gastroenterology, University of Amsterdam, Netherlands.
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1992 Dec) 166 (6) 1367-74.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921222

AB Gram-negative sepsis is caused by endotoxin-induced release of tumor necrosis factor (TNF) and other cytokines. HA-1A is a human monoclonal antibody that binds specifically to endotoxin. HA-1A should prevent death in endotoxemic patients and reduce serum levels of TNF and interleukin-6 (IL-6). This hypothesis was tested in 82 septic patients who were randomly allocated to receive a single intravenous 100-mg dose of HA-1A or placebo. Pretreatment endotoxemia was detected in 27 patients (33%). Death occurred within 28 days of treatment in 8 (73%) of 11 placebo recipients and in 5 (31%) of 16 HA-1A recipients (P = .02). The median decrease in serum TNF level 24 h after treatment was 12 ng/L in patients given HA-1A and 0 ng/L in placebo recipients (n = 65; P = .04). For IL-6, this was 204 ng/L in patients given HA-1A and 44 ng/L in placebo recipients (n = 67; P = .4). Thus, HA-1A reduces mortality in septic patients with endotoxemia and lowers serum TNF levels.

L6 ANSWER 38 OF 43 MEDLINE
DUPLICATE 34
ACCESSION NUMBER: 93101937 MEDLINE
DOCUMENT NUMBER: 93101937
PubMed ID: 1465578
TITLE: Kinetics of serum levels of interleukin-6 in Staphylococcus aureus septicemia.
AUTHOR: Soderquist B; Sundqvist K G; Vikerfors T
CORPORATE SOURCE: Department of Infectious Diseases, Orebro Medical Center Hospital, Sweden.
SOURCE: SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES, (1992) 24 (5) 607-12.
Journal code: 0215333. ISSN: 0036-5548.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 19930205
Last Updated on STN: 19970203
Entered Medline: 19930121

AB The kinetics of Il-6 serum concentrations were analyzed in 17 patients with a culture verified Staphylococcus aureus septicemia. The analyses were performed using an antigen capture immunoassay. All patients had elevated IL-6 serum concentrations on admission. In most cases a subsequent rapid decrease to low levels was registered within 10 days. The IL-6 serum concentrations reflected the clinical course. In sera sampled on admission a relationship was found between IL-6 serum concentrations and levels of C-reactive protein.

L6 ANSWER 39 OF 43 MEDLINE
DUPLICATE 35
ACCESSION NUMBER: 92306319 MEDLINE
DOCUMENT NUMBER: 92306319
PubMed ID: 1611704

TITLE: Polymicrobial sepsis selectively activates peritoneal but not alveolar macrophages to release inflammatory mediators (interleukins-1 and -6 and tumor necrosis factor).
AUTHOR: Ayala A; Perrin M M; Kisala J M; Ertel W; Chaudry I H
CORPORATE SOURCE: Department of Surgery, Michigan State University, East Lansing 48824.
CONTRACT NUMBER: R01 GM 37127 (NIGMS)
SOURCE: CIRCULATORY SHOCK, (1992 Mar) 36 (3) 191-9.
Journal code: 0414112. ISSN: 0092-6213.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920807
Last Updated on STN: 19920807
Entered Medline: 19920727
AB While a number of clinical studies indicate that elevated serum cytokine [interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF)] levels are associated with enhanced mortality in sepsis, the time course and the role that different macrophage (M phi) populations play in releasing these cytokines remain to be determined. To study this, polymicrobial sepsis was induced in C3H/HeN mice by cecal ligation and puncture (CLP). The animals were then sacrificed at 1, 4, or 24 hr post-CLP. Blood was taken for serum cytokine level determination. Macrophages, of either peritoneal (PM phi) or alveolar (AM phi) origin, were harvested by lavage, and their innate vs. inducible cytokine productive capacities were assessed by incubation with or without endotoxin (lipopolysaccharide; LPS). Serum levels of TNF were significantly enhanced 1 hr post-CLP (CLP = 3.8 +/- 2.4* vs. sham = 0.4 +/- 0.9 U/ml; P less than 0.05 by t test). However, not until 4 hr post-CLP were marked increases in IL-6 observed (CLP = 318.0 +/- 209.0* vs. sham = 1.1 +/- 0.5 U/ml), which remained elevated through 24 hr post-CLP (CLP = 11.3 +/- 15.0* vs. sham = 0.03 +/- 0.02 U/ml). Cytokine release (IL-1, IL-6, TNF) from PM phi (without the addition of LPS) was detectable only in cells harvested 1 h following CLP. Alveolar M phi from septic mice showed little in vivo activation. Septic PM phi IL-1 and IL-6 production was markedly depressed at all time points with LPS stimulation, but TNF release remained unaltered.(ABSTRACT TRUNCATED AT 250 WORDS)

L6 ANSWER 40 OF 43 MEDLINE DUPLICATE 36
ACCESSION NUMBER: 93047045 MEDLINE
DOCUMENT NUMBER: 93047045
PubMed ID: 1423922
TITLE: Production of tumor necrosis factor-alpha and interleukin-6 in mice infected with group B streptococci.
AUTHOR: Teti G; Mancuso G; Tomasello F; Chiofalo M S
CORPORATE SOURCE: Istituto di Microbiologia, Facolta di Medicina, Universita di Messina, Italy.
SOURCE: CIRCULATORY SHOCK, (1992 Oct) 38 (2) 138-44.
Journal code: 0414112. ISSN: 0092-6213.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921211
AB Group B streptococci (GBS) are a leading cause of sepsis and meningitis in neonates. Since cytokines are thought to play an important role in septic shock, we have studied serum levels of

tumor necrosis factor-alpha (TNF alpha) and interleukin-
6 (IL-6) in BALB/c mice infected with type III GBS. TNF alpha and
IL-6 were detected by the L929 cytotoxicity and the B9 proliferation
assays, respectively, in serial serum samples obtained after infection.
After i.p. challenge with an LD50, serum TNF alpha rose above baseline
values as early as 3 hr, peaked at 7 hr, and returned to baseline values
at 20 hr. IL-6 serum levels rose concomitantly with
TNF alpha, peaking 8 hr after challenge. No serum TNF alpha activity was
detected in the course of sublethal infections. However, a transient rise
in TNF alpha levels was observed after i.v. inoculation of high numbers
(greater than or equal to 1 x 10(8) of heat-killed GBS. When groups of
mice were injected i.v. with a single dose of anti-TNF alpha rabbit serum
2 hr before challenge with an LD90 or LD30, no effect was noted in terms
of survival, although the serum TNF alpha peak was completely abrogated.
Serum TNF alpha does not seem to play an obligatory role in GBS-induced
lethality of adult mice. However, further studies are needed to assess
better the role of this cytokine in the pathogenesis of GBS sepsis

L6 ANSWER 41 OF 43 MEDLINE
DUPLICATE 37
ACCESSION NUMBER: 92351276 MEDLINE
DOCUMENT NUMBER: 92351276
PubMed ID: 1641756
TITLE: Spin trap salvage from endotoxemia: the role of cytokine
down-regulation.
AUTHOR: Pogrebniak H W; Merino M J; Hahn S M; Mitchell J B; Pass H
I
CORPORATE SOURCE: Thoracic Oncology Section, National Cancer Institute,
National Institutes of Health, Bethesda, MD 20892.
SOURCE: SURGERY, (1992 Aug) 112 (2) 130-9; discussion 138-9.
Journal code: 0417347. ISSN: 0039-6060.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920911
Last Updated on STN: 19920911
Entered Medline: 19920828
AB BACKGROUND. The spin trap alpha-phenyl-N-tert-butyl-nitrone (PBN) affords
protection from the lethality of septic (lipopolysaccharide) shock. We
hypothesized that PBN may work through down-regulation of the
sepsis-induced cytokine cascade. METHODS. C3H/HEN mice received 30
mg/kg lipopolysaccharide 15 minutes after pretreatment with PBN or
vehicle. Animals were monitored for differences in behavior,
histopathologic studies, survival, and serum levels of
tumor necrosis factor (TNF-alpha), interferon-gamma (IFN-gamma), and
interleukin-6 (IL-6) after lipopolysaccharide. Northern
blot analyses of TNF, IFN-gamma, c-fos, and IL-6 transcripts were also
performed. RESULTS. Seventy-two-hour survival was significantly higher in
the PBN-treated (59/60) compared with the saline-treated animals (13/60;
p2 less than 0.005), and the PBN group exhibited a blunted endotoxemic
response. TNF levels were significantly lower in the PBN-treated animals
at 1 to 6 hours, whereas IFN-gamma levels were depressed at 8 hours. PBN
down-regulated TNF transcription at 30 minutes, with maximum lowering of
all cytokine transcripts at 6 hours. PBN depressed c-fos transcription
within 15 minutes of lipopolysaccharide injection. CONCLUSIONS. Spin trap
protection from endotoxemia may be related to interruption of the cytokine
network, with profound effects on transcription and protein elaboration.
Such compounds may prove useful in not only sepsis but also
other cytokine-free radical-related pathophysiologic alterations.

L6 ANSWER 42 OF 43 MEDLINE
DUPLICATE 38
ACCESSION NUMBER: 91127631
MEDLINE
DOCUMENT NUMBER: 91127631
PubMed ID: 1992764
TITLE: In vivo biologic and immunohistochemical analysis of interleukin-1 alpha, beta and tumor necrosis factor during experimental endotoxemia. Kinetics, Kupffer cell expression, and glucocorticoid effects.
AUTHOR: Chensue S W; Terebuh P D; Remick D G; Scales W E; Kunkel S L
CORPORATE SOURCE: Department of Pathology, Veterans Affairs Medical Center, Ann Arbor, MI 48105.
CONTRACT NUMBER: HL31237 (NHLBI)
HL31963 (NHLBI)
HL35276 (NHLBI)
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (1991 Feb) 138 (2) 395-402.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910405
Last Updated on STN: 19970203
Entered Medline: 19910314
AB Using a model of sepsis induced by parenteral challenge of mice with bacterial lipopolysaccharide (LPS), the authors analyzed the in vivo expression of interleukin-1 (IL-1) alpha,beta and tumor necrosis factor (TNF). Both TNF and IL-1 alpha,beta were detected in hepatic sinusoidal macrophages (Kupffer cells), immunohistochemically. Kinetic analysis showed a clear sequence of synthesis. Tumor necrosis factor was produced first, reaching maximal expression at 1 hour after LPS challenge, then rapidly disappeared. IL-1 beta followed, reaching maximal expression at 2 to 3 hours, then dropped off by 6 hours. Interleukin-1 alpha expression reached a peak at 6 hours and had disappeared by 18 hours. Analysis of serum bioactivity also revealed sequential expression that correlated with immunohistochemical findings. Tumor necrosis factor was maximal at 1 hour and IL-1 at 6 hours. The IL-1 bioactivity was not due to interleukin-6 (IL-6), as this was depleted from specimens by immunoabsorption. Also IL-6 bioactivity reached maximal levels at 3 hours, earlier than IL-1. Pretreatment with 4 mg/kg dexamethasone significantly decreased Kupffer cell expression of TNF and IL-1 alpha (about 80% and 60% suppression, respectively) but had less effect on IL-1 beta expression (about 30% suppression). Accordingly, serum levels of TNF were suppressed by 75% while serum IL-1 was decreased by 39%, indicating differential sensitivity of these cytokines to glucocorticoids. Endogenous corticosteroid levels increased as TNF levels decreased, supporting the contention that glucocorticoids regulate TNF synthesis. In contrast, IL-1 levels rose concurrently with corticosterone. These data indicate a sequential activation of cytokine gene expression in vivo, which may be critical to the cascade of events leading to septic shock, and provide evidence that Kupffer cells are a major source of cytokines in endotoxemia. Finally, the differential sensitivity of cytokine expression to glucocorticoids may in part explain the inadequacy of the latter in the treatment of sepsis.

L6 ANSWER 43 OF 43 MEDLINE
DUPLICATE 39
ACCESSION NUMBER: 90228909
MEDLINE
DOCUMENT NUMBER: 90228909
PubMed ID: 2184115
TITLE: Excessive in vitro bacterial lipopolysaccharide-induced

production of monokines in cirrhosis.
AUTHOR: Deviere J; Content J; Denys C; Vandenbussche P; Schandene L; Wybran J; Dupont E
CORPORATE SOURCE: Department of Gastroenterology, Hopital Erasme, Brussels Free University, Belgium.
SOURCE: HEPATOLOGY, (1990 Apr) 11 (4) 628-34.
Journal code: 8302946. ISSN: 0270-9139.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900706
Last Updated on STN: 19900706
Entered Medline: 19900525
AB The objective of this study was to analyze monokine production by peripheral blood mononuclear cells from patients with alcoholic cirrhosis.
The capacity of peripheral blood mononuclear cells and purified monocytes from these patients to produce tumor necrosis factor alpha, interleukin 1 beta, and interleukin 6 was investigated. Spontaneous production of tumor necrosis factor alpha, interleukin 6 and interleukin 1 beta was similar in cirrhotic and healthy subjects, but serum levels of interleukin 6 (less than 2 U/ml vs. 9.5 +/- 3 U/ml) and tumor necrosis factor alpha (3.1 +/- 1.2 pg/ml vs. 12.0 +/- 1.2 pg/ml) were significantly higher in cirrhotic patients. However, peripheral blood mononuclear cells or purified monocytes from patients with alcoholic liver cirrhosis, stimulated in vitro with Escherichia coli lipopolysaccharide, displayed a marked increase of tumor necrosis factor alpha, interleukin 1 beta and interleukin 6 secretions compared with healthy controls.
A striking feature of this overproduction was its reversibility as assessed by allowing cells to rest in vitro without lipopolysaccharide for 1 to 7 days before stimulation. In such conditions, tumor necrosis factor alpha and interleukin 6 secretions declined to levels present in healthy subjects in whom production remained stable, whereas interleukin 1 beta secretion markedly decreased in both groups to the point where no difference could be seen. This reversible oversecretion of cytokines after lipopolysaccharide stimulation, along with the lack of abnormality of spontaneous cytokine secretion, suggests that monocytes in these patients may have undergone an in vivo activation process analogous to a priming phenomenon. The in vitro activation with lipopolysaccharide may represent the correlate of in vivo endotoxemia observed during acute events such as sepsis.(ABSTRACT TRUNCATED AT 250 WORDS)

=> s tnf (W) antibodies or tumor (W) necrosis (w) factor (w) antibodies
4 FILES SEARCHED...
L7 891 TNF (W) ANTIBODIES OR TUMOR (W) NECROSIS (W) FACTOR (W) ANTIBODI
ES

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YOU HAVE REQUESTED DATA FROM 1 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 1 CAPLUS
COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:842658 CAPLUS
DOCUMENT NUMBER: 123:225947
TITLE: Use of anti-TNF antibodies as drugs in treating diseases involving elevated interleukin-6 serum levels
INVENTOR(S): Stenzel, Roswitha; Kaul, Martin; Daum, Lothar; Kempeni, Joachim; Raab, Christa; Schaefer, Sibylle
PATENT ASSIGNEE(S): Knoll A.-G., Germany
SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
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WO 9520978 A1 19950810 WO 1995-EP291 19950127
W: AU, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, MX, NO, NZ, PL, RU, SI, UA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
DE 4409513 C1 19951019 DE 1994-4409513 19940319
IL 112427 A1 19981206 IL 1995-112427 19950124
CA 2182723 AA 19950810 CA 1995-2182723 19950127
AU 9515201 A1 19950821 AU 1995-15201 19950127
CN 1140414 A 19970115 CN 1995-191517 19950127
JP 09509411 T2 19970922 JP 1995-520363 19950127
BR 9506741 A 19971021 BR 1995-6741 19950127
EP 804236 A1 19971105 EP 1995-906353 19950127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI
HU 76875 A2 19971229 HU 1996-2169 19950127
TW 403656 B 20000901 TW 1995-84100744 19950127
CZ 290843 B6 20021016 CZ 1996-2322 19950127
ZA 9500956 A 19951011 ZA 1995-956 19950207
FI 9603101 A 19960806 FI 1996-3101 19960806
NO 9603280 A 19961004 NO 1996-3280 19960806
MX 9603243 A 20000228 MX 1996-3243 19960807
US 6235281 B1 20010522 US 1996-687328 19960807
AU 9915495 A1 19990401 AU 1999-15495 19990208
US 2001010819 A1 20010802 US 2001-782290 20010214
PRIORITY APPLN. INFO.: DE 1994-4403669 A 19940207
DE 1994-4409513 A 19940319
AU 1995-15201 A3 19950127
WO 1995-EP291 W 19950127
US 1996-687328 A1 19960807
AB Tumor necrosis factor (TNF) antagonists, esp. anti-TNF
antibodies and their fragments, are useful in prodn. of drugs to
treat diseases characterized by elevated interleukin-6
serum levels, e.g. sepsis.

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COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY
SESSION
FULL ESTIMATED COST
63.46 63.67

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
ENTRY
SESSION
CA SUBSCRIBER PRICE
-3.91 -3.91

STN INTERNATIONAL LOGOFF AT 18:14:53 ON 19 MAR 2003

TITLE: Significance of systemic inflammatory response syndrome at cardiopulmonary bypass.
AUTHOR: Furunaga A; Tsuboi H; Itoh H; Kawamura T; Minami Y; Gohra H; Katoh T; Fujimura Y; Esato K
CORPORATE SOURCE: First Department of Surgery, Yamaguchi Univeristy School of Medicine, Ube, Japan.
SOURCE: NIPPON KYOBU GEKA GAKKAI ZASSHI. JOURNAL OF THE JAPANESE ASSOCIATION FOR THORACIC SURGERY, (1996 Jun) 44 (6) 790-4.
Journal code: 19130180R. ISSN: 0369-4739.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960924
Last Updated on STN: 19960924
Entered Medline: 19960917
AB Systemic Inflammatory Response Syndrome (SIRS) is a new concept of entry criteria for sepsis. This concept, when applied to area of Multiple Organ Failure (MOF), is considered to be a preparatory state for MOF. To study the significance of SIRS state at cardiac surgery, we measured the body temperature, white blood cell count, respiratory rate and heart rate of 18 patients who underwent elective cardiac surgery, from the 1st post-operative day to the 7th post-operative day. We also measured Interleukin-6 and 8 (IL-6 and IL-8) to understand the relationship between the SIRS state and inflammatory cytokines just after cardiopulmonary bypass (CPB), at the 1st, 3rd and 6th postoperative day. The result was as follows: Patients with CPB more than 120 minutes have more frequency and longer duration of SIRS than patients with CPB less than 120 minutes. Serum levels of IL-8 at SIRS state were revealed statistically higher than at non-SIRS case. Duration of SIRS state was related to CPB time and serum levels of IL-6 and IL-8 just after CPB. We concluded that SIRS state is an indication for anti-cytokine therapy to prevent MOF, and it is important to shorten CPB time in order to decrease the duration of SIRS.

L6 ANSWER 27 OF 43 MEDLINE DUPLICATE 24
ACCESSION NUMBER: 97048569 MEDLINE
DOCUMENT NUMBER: 97048569
PubMed ID: 8893405
TITLE: Dynamics of blood cytokine concentrations in patients with bacteremic infections.
AUTHOR: Kragsbjerg P; Holmberg H; Vikerfors T
CORPORATE SOURCE: Department of Infectious Diseases, Orebro Medical Center Hospital, Sweden.
SOURCE: SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES, (1996) 28 (4) 391-8.
Journal code: 0215333. ISSN: 0036-5548.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970128
AB Cytokines play a major role in the pathophysiology of sepsis and septic shock. Using enzyme immunoassays the acute serum levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha), granulocyte-colony stimulating factor (G-CSF), interleukin-8 (IL-8), and leukemia inhibitory factor (LIF) were investigated in 90 patients with positive blood cultures and clinical signs of infection. In 27 patients samples were obtained on admission, after 1, 4, 12, 18, and 24 h, and then daily. The acute serum

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levels of IL-6, TNF-alpha, G-CSF, and IL-8 were significantly
higher among patients with severe sepsis. Patients with
Gram-negative infection had significantly higher levels of TNF-alpha on
admission than did patients with Gram-positive infections (p = 0.0008).
The levels of IL-6, G-CSF and, to some extent, TNF-alpha decreased rapidly
in survivors within the first 24 h of admission to hospital and
institution of treatment. LIF was detected in 8/90 in both survivors and
nonsurvivors.

L6 ANSWER 28 OF 43 EMBASE
COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 25
ACCESSION NUMBER: 97046690 EMBASE
DOCUMENT NUMBER: 1997046690
TITLE: [The role of cytokines in the diagnosis of sepsis].
STELLENWERT VON ZYTOKINEN IN DER SEPSIS-DIAGNOSTIK.
AUTHOR: Fraunberger P.; Walli A.K.; Seidel D.
CORPORATE SOURCE: Dr. P. Fraunberger, Institut fur Klinische Chemie, Klinikum
Grosshadern, Universitat Munchen, Marchioninistrasse 15,
D-81366 Munchen, Germany
SOURCE: Infusionstherapie und Transfusionsmedizin, (1996) 23/SUPPL.
4 (109-116).
Refs: 77
ISSN: 1019-8466 CODEN: IRANEE
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: German
SUMMARY LANGUAGE: German; English
AB Both clinical and experimental studies show that cytokines play a central
role in sepsis. Inflammatory conditions lead to release of
cytokines which coordinate various components of the immune system. Even
though several cytokines are involved in the complex process of the
development of sepsis, only interleukin 1 (IL-1),
interleukin 6 (IL-6), tumor necrosis factor alpha (TNF),
interleukin 8 (IL-8) and interleukin 10 (IL-10) can be measured accurately
with the facilities available in clinical laboratories. Certain cytokine
antagonists such as soluble TNF receptors and interleukin 1 receptor
antagonist are also found in measurable amounts in serum. Serum
levels of IL-6 appear to correlate with the organ dysfunction and
have high prognostic value. Even though TNF plays a central role in
sepsis, the serum levels show considerable
variation owing to its short biological half life and therefore render
this parameter less suitable for the follow-up of sepsis. Recent
studies show the usefulness of the measurement of TNF receptors in
sepsis. These receptors have a longer biological half life than
TNF and can be measured within a few hours by automated methods in a
routine clinical chemistry laboratory.

L6 ANSWER 29 OF 43 CAPLUS
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ACCESSION NUMBER: 1995:842658 CAPLUS
DOCUMENT NUMBER: 123:225947
TITLE: Use of anti-TNF antibodies as drugs in treating
diseases involving elevated interleukin-6 serum levels
INVENTOR(S): Stenzel, Roswitha; Kaul, Martin; Daum, Lothar;
Kempeni, Joachim; Raab, Christa; Schaefer, Sibylle
PATENT ASSIGNEE(S): Knoll A.-G., Germany
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION: